REMARKS

An Office Action was mailed in the above-referenced matter on August 28, 2009. Claims 1, 3, 5-10, and 19-22 were pending in the Application. Claims 1, 3, 5-10, and 19-22 were rejected. Claim 1 has been cancelled. Claims 3, 5, 9, 19-22 have been amended and new claims 23-31 have been added. All of the dependent claims are now dependent upon amended independent claim 21 (dependent claims 3, 5-10, 19 and 20) or independent claim 22 (new claims 23-31) and correspond to the previously pending claims 3, 5-10, 19 and 20 which were dependent upon claim 1. Claims 21 and 22 have been amended wherein the "fixing" step has been amended to include the further limitation of "dry fixation". Support for this amendment can be found on page 18, line 1; page 37, line 23 to page 38, line 4 (in example 1); and page 43 lines 12-18 (in example 2) in the specification. It is believed that none of these amendments constitute new matter.

Interview Summary

On August 25, 2009, Examiner Christopher Babic, Applicant's Representatives Darla A. Graff and Angela M. Domitrovich, participated in a telephone interview concerning U.S. Application No. 10/588,597. During the interview Claims 1, 21 and 22, as well as the prior art reference of Hu (US 5,939,251) were discussed. During this interview, potential claim amendments in view of the prior art reference of Hu were discussed. An agreement to allowable claims was not reached; however, Applicant has taken the Examiner's comments into account in the preparation of this response.

Rejection Under 35 U.S.C § 112-indefiniteness

The Examiner has rejected Claims 1, 3, 5-10, 19 and 20 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office action states that the recitation of "the target nucleic acid" in the final "wherein" clause in Claim 1 has insufficient antecedent basis. Applicants have canceled Claim 1 and therefore the rejection is now moot.

Rejection Under 35 U.S.C. § 102(b) Hu

The Examiner has maintained the rejection of Claims 1, 3, 9-10 and 19 under 35 U.S.C. § 102(b) as being anticipated by Hu (U.S. Patent No. 5,939,251). Applicants have canceled Claim 1, amended Claims 3, 9, 10 and 19 to be dependent upon amended Claim 21 and have added new Claims 23-31, which are dependent upon amended Claim 22. Applicants contend that in view of these amendments, this rejection is now moot and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 103(a) Hu in view of Villeponteau et al.

The Examiner has maintained the rejection of Claims 5 and 20 under 35 U.S.C. § 103(a) as being unpatentable over Hu (U.S. Patent No. 5,939,251) in view of Villeponteau et al. (U.S. Patent No. 5,776,679).

Applicants have canceled Claim 1 in which Claims 5 and 20 previously depended upon. Claims 5 and 20 have now been amended to be dependent upon amended Claim 21. Applicants contend that in view of these amendments, this rejection is now moot and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 103(a) Hu in view of Villeponteau et al. in further view of Stapleton et al.

The Examiner has maintained the rejection of Claims 6-8 under 35 U.S.C. § 103(a) as being unpatentable over Hu (U.S. Patent No. 5,939,251) in view of Villeponteau et al. (U.S. Patent No. 5,776,679) as applied to Claim 5 and in further view of Stapleton et al. (U.S. Patent No. 6,103,192).

Applicants have canceled Claim 1 in which Claims 6-8 previously depended upon. Claims 6-8 have been amended to be dependent upon amended Claim 21. Applicants contend that in view of these amendments, this rejection is now moot and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 103(a) Nuovo et al., in view of Hu

The Examiner has rejected Claims 21 and 22 under 35 U.S.C. § 103(a) as being unpatentable over Nuovo et al., (*Genome Res.* 1993 2:305-312) in view of Hu (US Patent 5,939,251). The Office action reasons that Claims 21 and 22 "require that amplified nucleic acid exist in the PCR solution outside the cell" and that with regard to the "fixing", "pre-treating", and "performing" steps, Nuovo teaches performing *in situ* PCR. The Office action concludes that it would have been *prima facie* obvious to utilize the products and methods of Hu to perform the *in situ* PCR methods of Nuovo since the prior art expressly recognizes that such PCRs could be performed more efficiently within such products. The Examiner does note that Nuovo does not expressly teach divided compartments of a support.

Applicants have amended Claims 21 and 22 to include the further limitation of "dry fixation" in the "fixing" step. As discussed below, neither Hu nor Nuovo teach nor suggest this further limitation to the methods of the present invention.

A *prima facie* case of obviousness has three distinct requirements. First, the references must teach or suggest every claim element. M.P.E.P. §§ 2142 and 2143.03. Second, there must be a motivation to modify or combine the teachings of the cited references. M.P.E.P. §§ 2143 and 2143.01. Third, there must be a reasonable expectation of success in performing the modified or combined teachings of the references. M.P.E.P. § 2143.02.

Applicants contend that neither Hu nor Nuovo teach or suggest the step of fixing a cell-containing sample directly on divided compartments of a support by **dry fixation**. As previously discussed, Hu teaches an *in situ* PCR detection method. Nuovo also discloses *in situ* PCR and the different variables for enhancing *in situ* detection (see Nuovo, abstract). As discussed in the previous response, *in situ* PCR detection is a method for detecting intracellular localization of a target nucleic acid. *In situ* is an improvement of an *in situ* hybridization method (ISH) that was developed to detect a nucleic acid amplified in a cell while maintaining the conformation of the cell (see pg. 3, lines 12-18 of the specification). In both of these methods, it is known by those of skill in the art that the cell morphology should be maintained for the best PCR amplification to occur and thus fixation methods which help to maintain cell morphology are utilized. These

types of fixation methods include formalin fixation and glutaraldehyde fixation. Nuovo teaches that the choice of fixative is a critical factor that influences the outcome of in PCR amplification. As shown in Tables 2 and 3 of Nuovo, *in situ* PCR detection of amplified DNA varies depending upon the fixation method used and that samples that are fixed by treatment with **formalin** produced the highest detection rates. In addition, Hu describes that *in situ* PCR processes are typically performed on sample tissues or cells which are fixed by treatment with formalin (colm 1, lines 63-65) as well as disclosing that the tissue or cell specimens in the *in situ* PCR method taught were paraffinized or frozen (colm 5, lns 7-8 of Hu).

In contrast, the method of the present invention is characterized by using a different fixation method (i.e. **dry fixation,** see Examples 1 and 2 in the specification) from that disclosed by both Hu and Nuovo (i.e. formalin fixation). As mentioned above, maintaining cell morphology is known by those of skill in the art to be important to the *in situ* detection methods described by Hu and Nuovo and can not be achieved by dry fixation of the sample. Nuovo clearly shows that fixation with ethanol or acetone **reduced** the detection rate and therefore Nuovo teaches away from using other fixation agents or procedures. Since Nuovo discloses that the highest detection rate is achieved using formalin for the fixation step, there is no motivation to modify Nuovo's teachings to the include the dry fixation step of the method of the present invention. In addition, the detection procedure of PCR products by gel electrophoesis as disclosed by Nuovo is merely a procedure to confirm whether the amplification by PCR was correctly performed under the aforementioned conditions. Such description also does not teach or suggest use of dry fixation as claimed.

Applicants contend that neither Hu nor Nuovo teach or suggest the step of dry fixation and that since neither of these references alone or in combination teach each and every element of Claims 21 or 22, Applicants submit that Claims 21 and 22 are patentable over the cited references. The Applicants respectfully request that the rejection under 35 U.S.C 103 be withdrawn.

Closing Remarks

Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-1970, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-1970.

Respectfully submitted,

SHERIDAN ROSS P.C.

By: /Angela M. Domitrovich/
Angela M. Domitrovich
Registration No. 62,948
1560 Broadway, Suite 1200
Denver, Colorado 80202-5141
(303) 863-9700

Date: March 1, 2010